

Remarks

I. Status of the Claims

Claims 1, 3-9, and 11-13 were pending at the time of the Office Action. No claims have been amended. Therefore, claims 1, 3-7, 9, and 11-13 remain pending.

II. Claims 1, 3-9, and 11-13 Are Patentable Over the Cited References

Claims 1, 3-9, and 11-13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Wu (*J. Pathol.*, 195(1):53-65, 2001; IDS file 2/27/04, Entry C13), in view of Shaffer (*Annual Review of Psychology*, Vol. 46, p. 561-584, 1995), in view of Nath et al. (*Br J Clin Pharmacol*, Vol. 52, p. 671-680, 2001), in view of Cole et al. (*Prenatal Diagnosis*, Vol. 19, p. 351359, 1999), and in view of deGroot et al. (*Analytica Chimica Acta*, Vol. 446, p. 71-83, 2001). Claims 1 and 7 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the above-listed references, and further in view of Jensen et al. (*Bioinformatics*, Vol. 16, No. 4, p. 326-333, 2000). Applicants respectfully traverse because the rejection is legally insufficient and because the pending claims are patentably distinct over the cited combination.

A. The Office's Response to Arguments

The Office Action stated that "Applicant's arguments filed 23 July 2009 have been fully considered but they are not persuasive." At the outset, Applicants note that the current rejection includes an additional reference—the Nath reference—which Applicants had no opportunity to address in the prior response. Applicants are particularly confused by the addition of the Nath reference because they do not believe that the prior amendment substantively changed the scope of the claims, and as noted in the remarks accompanying the prior amendment, did not believe it

would necessitate further search. As the Office is aware, piecemeal examination should be avoided. MPEP 707.07(g).

B. The Office Action Impermissibly Re-Writes and Re-Characterizes the Claims

The rejection is improper because it depends on an improper summary of nine of the ten pending claims. “Distilling an invention down to the ‘gist’ or ‘thrust’ of an invention disregards the requirement of analyzing the subject matter ‘as a whole.’” MPEP § 2141.02(II); *see also W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984); *Bausch & Lomb v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 447-49, 230 USPQ 416, 419-20 (Fed. Cir. 1986), cert. denied, 484 U.S. 823 (1987). The Action at page 4 improperly distills all of claims 1, 3-6, 9, and 11-13 into a single paragraph.

The Office further oversimplifies claims 11 and 13 by implying that they recite “the iterative removal of outliers.” Action at 7. However, claims 1 and 13 recite: “*adjusting the plurality of expression profiles* of the control group and the plurality of expression profiles of the experimental group, *the adjusting comprising: identifying outliers* in the plurality of expression profiles of the control group and the plurality of expression profiles of the experimental group; *and re-scaling* the plurality of expression profiles of the control group and the plurality of expression profiles of the experimental group to an averaged profile of the control group to diminish or exclude influence of the identified outliers” (emphasis added).

As another example, the Office oversimplifies claims 1 and 13 by implying that they simply recite a T-test. However, claims 1 and 13 recite an associative T-test comprising “a T-test in which a plurality of *replicated residuals for each gene of the plurality of the expression profiles of the experimental group are compared with an entire set of residuals from the plurality of expression profiles of the control group*” (emphasis added).

Additionally, the rejection does not individually address each of claims 1, 3-6, 9, and 11-13, such that Applicant is precluded from addressing the application—or lack thereof—of the prior art to dependent claims 3-6, 9, and 11-12. For brevity, Applicants will not dissect the entire rejection, but respectfully submit that the rejection is improper at least because the over-generalization of the claims has apparently caused the Office to overlook several features of the claims, thereby preventing the examination of each claim *as a whole*.

C. The Rejection Did Not Address Every Feature of the Claims

“In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious.” MPEP § 2141.02(I) (citing *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenck v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983)); *see also* 35 U.S.C. § 103(a).

“All words in a claim must be considered in judging the patentability of that claim against the prior art.” *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). Section 2143.03 of the MPEP requires the “consideration” of every claim feature in an obviousness determination. As the BPAI also recently confirmed, a proper obviousness determination requires that an Examiner make “a searching comparison of the claimed invention – *including all its limitations* – with the teaching of the prior art.” *See In re Wada and Murphy*, Appeal 2007-3733 (Jan. 14, 2008), *citing In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995).

But the Office Action did not fully address explicit features that appear in both of independent claims 1 and 13, including at least the following emphasized features of claim 1:

1. A method of associative analysis, comprising:
collecting a plurality of expression profiles of a control group and a plurality of expression profiles of an experimental group;

normalizing the plurality of expression profiles of the control group relative to their backgrounds;

normalizing the plurality of expression profiles of the experimental group relative to their backgrounds;

adjusting the plurality of expression profiles of the control group and the plurality of expression profiles of the experimental group, the adjusting comprising:

identifying outliers in the plurality of expression profiles of the control group and the plurality of expression profiles of the experimental group; and

re-scaling the plurality of expression profiles of the control group and the plurality of expression profiles of the experimental group to an averaged profile of the control group to diminish or exclude influence of the identified outliers;

identifying a group of similarly expressed genes, defining a reference group, determined from the plurality of expression profiles of the control group;

identifying a plurality of differentially expressed genes in the plurality of expression profiles of the experimental group based on the reference group, wherein identifying the plurality of differentially expressed genes comprises utilizing a paired T-test and an associative T-test, the associative T-test comprising a T-test in which a plurality of replicated residuals for each gene of the plurality of the expression profiles of the experimental group are compared with an entire set of residuals from the plurality of expression profiles of the control group; and

determining a classification of the differentially expressed genes as (a) likely false positive, (b) real positives, or (c) potential positives using the paired T-test and associative T-test, wherein determining the classification comprises:

classifying the genes identified as expressed by the paired T-test and not identified as expressed by the associative T-test as likely false positives;

classifying the genes identified as expressed by the paired T-test and the associative T-test as real positives; and

classifying the genes identified as expressed by the associative T-test and not identified as expressed by the paired T-test as potential positives; and

outputting the classified real positives to a user.

Because the Rejection does not fully address each and every claimed feature, the rejection is incomplete and therefore improper.

D. No Combination of the Cited References Would Include Every Claimed Feature

As noted above, “[i]n determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious.” MPEP § 2141.02(I) (citations omitted). For the Office to carry its burden of establishing a *prima facie* case of obviousness, however, the Supreme Court recently confirmed that “there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR Int’l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). As such, the asserted reference or references must teach or suggest *each and every claim feature* to a person of ordinary skill in the relevant art. See *In re Royka*, 490 F.2d 981 (CCPA 1974). The rejection of claims 1 and 13 should be withdrawn because no combination of the cited references would teach or suggest every claimed feature.

The Wu reference: The Office Action concedes that Wu does not show any of:

- an associative T-test, Action at 5;
- determining a classification for the identity of differentially expressed genes where genes identified by the T-test but not the Associative T-test are likely false positives, gene identified by the T-test and the associative T-test are real positives, and genes identified by the Associative T-test but not the T-test are potential positives, Action at 5-6;
- the diminishing or excluding the influence of outliers, Action at 6 (not even shown by Wu in combination with Cole, Nath, and Shaffer);

The Office attempts to supply the deficiencies with four more references—Cole, Nath, Shaffer, and deGroot. But this combination is deficient for at least the following reasons:

The Nath reference: The Office Action relies on Nath to show a “T-test of residuals, reading on an associative T-test (p.673, col. 2).” Action at 6. But Nath is directed to a study of “pharmacokinetics of amphotericin B in children with malignant diseases.” Nath’s discussion

of a T-test on column 2 of page 673 is limited to: “A number of evaluation criteria were then used to select the most appropriate [pharmacokinetic] model including . . . (6) residuals with a mean that was not significantly different from zero using a student’s T-test” In contrast, claims 1 and 13 explicitly recite that the associative T-test comprises “a T-test in which a plurality of replicated residuals *for each gene of the plurality of the expression profiles of the experimental group are compared with an entire set of residuals from the plurality of expression profiles of the control group*” (emphasis added). Nath simply does not disclose or suggest a T-test with the explicitly recited features of the present claims.

The deGroot reference: The Office Action relies on deGroot to show “the pre-processed data used to perform PCA to detect outliers (p.78, col. 2) . . . outliers have an effect on PCA and are removed, reading on outlier exclusion (p.78, col. 2- p. 79, col. 1) . . . PCA is repeated until no outliers are excluded (p.79, col. 1) . . . that by removing outliers PCA is easier.” Action at 7. The Office Action further states that it would have been obvious to one of ordinary skill “to exclude or diminish the influence of outliers in the method of gene analysis of Wu et al. in view of Cole et al. and in view of Shaffer by modifying the method with the iterative removal of outliers from the data of deGroot et al. because deGroot et al. shows removing the influence of outliers simplifies PCA by eliminating the data masking effect of the outliers.” Action at 7. But the Office oversimplifies the claims—claims 1 and 13 do not merely recite “the iterative removal of outliers.” Instead, claims 1 and 13 recite: “*adjusting the plurality of expression profiles of the control group and the plurality of expression profiles of the experimental group, the adjusting comprising: identifying outliers in the plurality of expression profiles of the control group and the plurality of expression profiles of the experimental group; and re-scaling the plurality of expression profiles of the control group and the plurality of expression profiles of the*

experimental group to an averaged profile of the control group to diminish or exclude influence of the identified outliers” (emphasis added). In contrast, deGroot describes *individually* identifying and *individually* removing outlying Raman spectra: “[a]ll other remote spectra in these two score-plots (114, 193, 287, and 289) contain also spikes and should be removed. The number of considered PCs is increased until no more outlying objects could be found. The detected outliers, due to spikes, are removed from the set of Raman spectra and PCA is repeated for the remaining spectra.” deGroot, p. 79, col. 1. As such, deGroot does not disclose or suggest “*adjusting the plurality of expression profiles . . . , the adjusting comprising: identifying outliers . . . ; and re-scaling the plurality of expression profiles of the control group and the plurality of expression profiles of the experimental group to an averaged profile of the control group to diminish or exclude influence of the identified outliers,*” as recited in independent claims 1 and 13 (emphasis added).

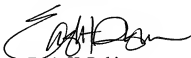
In view of the foregoing, Applicants respectfully submit that the rejection is incomplete, and therefore improper, at least because: (1) the rejection improperly distilled and re-wrote the claims; (2) the rejection did not address every explicit feature of the claims; and (3) no combination of the cited references would disclose or suggest every feature of the claims.

The Jensen reference fails to supply the deficiencies of the foregoing references. As such, claims 1 and 13 are nonobvious and patentable, and claims 2, 3-9, and 11-12 are also nonobvious and patentable at least because they depend from claim 1. See MPEP § 2143.03; *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Applicants therefore respectfully request reconsideration and withdrawal of the rejection.

III. Conclusion

Applicants believe that these remarks fully respond to all outstanding matters for this application, and respectfully submit that all claims are in condition for allowance. Should the Examiner have any questions regarding this submission, a telephone call to the undersigned at 512-536-3083 is respectfully invited.

Respectfully submitted,



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